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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,475	01/22/2002	Alexander Gaiger		3551

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EXAMINER

AEDER, SEAN E

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/057,475	GAIGER ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on 01 March 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 6 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

***Detailed Action***

The Amendments and Remarks filed 3/1/06 in response to the Office Action of 11/1/05 are acknowledged and have been entered.

Claim 6 was pending.

Claims 6 has been amended by Applicant.

Claim 6 is currently under examination.

The text of those sections of Title 35 U.S.C. code not included in this Office Action can be found in a prior Office Action.

***Objections Withdrawn***

The objection of claim 6 for missing an article before the word "nucleic" has been withdrawn in view of amendments.

***Response to Arguments***

Claim 6 remains rejected under 35 U.S.C. 112, second paragraph, because the claim is indefinite, for the reasons of record in the Office Action mailed 11/1/05 and the reasons set-forth below.

The Office Action of 11/1/05 contained the following text:

Claim 6 recites "a predetermined cut-off value" is to be used to determine the presence of cancer in a patient. It is unclear what this pre-determined cut-off value is or how it will be obtained.

In response the Office Action of 11/1/05, Applicant argues that the skilled artisan could readily determine an appropriate cut-off value for practicing the claimed methods. Applicant further points out that the specification provides guidance for determining a cut-off value and using a cut-off value in the claimed diagnostic methods (pages 125-128 of the specification). Thus, Applicant states that the present disclosure provides adequate guidance regarding the determination and selection of a cut-off value and, thus, provides reasonable clarity under 35 U.S.C., second paragraph, for the claimed method. Applicants further argue that the situation is analogous to claims directed to a therapeutically effective amount of a compound, where courts have recognized that determining effective dosage for a pharmaceutical agent against a particular disease is well within the ordinary skill in the art. *In re Bundy*, 209 U.S.P.Q. 48 (C.C.P.A. 1981).

The arguments found in the response of 3/1/06 have been carefully considered, but are deemed not to be persuasive. According to 35 U.S.C., second paragraph, the claims are required to particularly point out and distinctly claim the invention. As pointed out by Applicant, the specification discloses various non-limiting manners a "predetermined cut-off value" *could* be determined (paragraph bridging pages 127-128 of the specification). Thus, the instant claim remains indefinite since the specification does not disclose, nor does the claim recite, exactly how *the* predetermined cut-off value *will* be determined. It is unclear how the exact numeric value of the "predetermined cut-off value" *will* be determined. Further, as claimed, it is unclear whether a measured amount above this "predetermined cut-off value" is indicative of lymphoma, or whether a measured amount below this "predetermined cut-off value" is

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indicative of lymphoma. Further, the decision of *In re Bundy*, 209 U.S.P.Q. 48 (C.C.P.A. 1981) is not applicable to the instant situation. This is not an enablement issue; the rejection of the instant claim is not based on whether one of skill in the art would be able to do something. The instant claim is rejected because the claim does not indicate exactly *how* something is done.

Claim 6 remains rejected under 35 U.S.C. 112, first paragraph, because the claim does not provide enablement for a method for detecting the presence of every type of cancer, for the reasons of record in the Office Action mailed 11/1/05 and the reasons set-forth below.

The Office Action of 11/1/05 contained the following text:

Claim 6 is drawn to a method for determining the presence of every *and any type of cancer* in a patient comprising the step of comparing the amount of a polypeptide encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 or a complement thereof in a sample to a predetermined cut-off value.

The specification teaches that the polynucleotide sequence SEQ ID NO:10,582 was identified, using a combination of PCR subtracted cDNA libraries, microarray analyses, and RealTime PCR, as a gene with a similar tissue expression profile to CD20 and CD52 in lymphomas (Example 5, in particular). The specification further teaches that SEQ ID NO:10,582 is also termed Ly1448 (see Figure 9 and paragraph 576, in particular). The specification further teaches that higher levels of antibodies that interact with a polypeptide encoded by SEQ ID NO:10,582 are present in the sera of

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lymphoma patients as compared to normal controls (see Figure 31 and Example 13, in particular), which indicates that a polypeptide encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 could be used as a diagnostic marker for lymphomas. However, the specification does not demonstrate that a polypeptide encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 or a complement thereof could be used as a diagnostic marker for every type of cancer.

If a molecule such as a protein encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 or a complement thereof is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful clinical application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test

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the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the protein's expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the peptides in any diagnostic setting without undue experimentation.

The Applicants have presented sufficient data demonstrating that detection of a protein encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 could be used as a diagnostic marker for lymphomas, but the Applicants have not demonstrated that expression of a protein encoded by a nucleic acid comprising the sequence set forth in SEQ ID NO:10,582 could be used as a marker for any other type of cancer. Further, one of skill in the art would recognize that the lymphomas differ greatly from most other cancers. Lymphomas involve circulating lymphocytes of the lymphatic system; In contrast, the majority of other cancers are carcinomas, which are epithelial in origin. Additionally, etiologies of lymphomas differ from those of other types of cancers, lymphomas require different methods for treatment

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than other types of cancers, and lymphomas involve methods of detection distinct from other types of cancer.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

In response the Office Action of 11/1/05, Applicant has amended the preamble of the claim to recite: "A method for detecting the presence of ~~a cancer~~ lymphoma in a patient, comprising the steps of...".

The amendment to claim 6 has been carefully considered, but is deemed not to be sufficient to overcome the rejection. It is noted that the amended claim concludes by reciting: "...comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of **a cancer** in the patient". In the response of 3/1/06, Applicant did not present evidence or argue that the claimed method would detect the presence of any cancer other than lymphomas. Therefore, for the reasons stated in the previous Office Action, this claim remains rejected because the claimed method is not enabling for detecting every type of cancer. It is suggested that Applicant replace the words "a cancer" with "lymphoma".

### ***Summary***

No claim is allowed.



***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a). A shortened statutory period for response to this Final Action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this Final Action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. '1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than six months from the date of this Final Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

  
JEFFREY SIEW  
SUPERVISORY PATENT EXAMINER

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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